Claims

- 1. A remedy and/or a preventive of a chronic disease comprising an EDG-2 antagonist.
- 2. The remedy and/or the preventive according to claim 1, wherein the chronic disease is chronic asthma, glomerular nephritis, obesity, prostate hyperplasia, a disease induced by the progress of arteriosclerosis, rheumatoid or atopic dermatitis.
- 3. The remedy and/or the preventive according to claim 2, wherein the chronic disease is prostate hyperplasia.
- 4. The remedy and/or the preventive according to claim 1, wherein the EDG-2 antagonist is a β -alanine derivative of formula (I)

$$(R^{2a})_{ma}$$

$$R^{4a}$$

$$N$$

$$R^{5a}$$

$$R^{5a}$$

$$R^{5a}$$

$$R^{4a}$$

$$R^{5a}$$

$$R^{5a}$$

$$R^{7a}$$

wherein A^a is, (1) C1-6 alkylene, (2) C2-6 alkenylene, or (3) C2-6 alkynylene, wherein A^a may be substituted with 1-3 of C1-4 alkyl.

Cyc1^a is, (1) C3-15 carboring, or (2) 3-15 membered heteroring having 1-4 of nitrogen, 1-2 of oxygen and/or 1-2 of sulfur,

 $R^{1a} \text{ is (1) C1-4 alkyl, (2) halogen, (3) cyano, (4) trihalomethyl, (5) -OR^{6a}, (6) -SR^{7a}, (7) -NR^{8a}R^{9a}, (8) \text{ nitro, (9) -COOR}^{10a}, (10) -CONR^{11a}R^{12a}, (11) -NR^{13a}COR^{14a}, (12) -SO_2NR^{15a}R^{16a}, (13) -NR^{17a}SO_2R^{18a}, (14) -S(O)R^{19a}, \text{ or (15) -SO}_2R^{20a},$

 R^{6a} , R^{7a} , R^{8a} , R^{9a} , R^{10a} , R^{11a} , R^{12a} , R^{13a} , R^{14a} , R^{15a} , R^{16a} , R^{17a} , R^{18a} , R^{19a} and R^{20a} are each independently, (1) hydrogen, or (2) C1-4 alkyl,

 R^{2a} and R^{3a} are each independently, (1) C1-4 alkyl, (2) C1-4 alkoxy, or (3) halogen,

R^{4a} and R^{5a} are each independently, (1) hydrogen, (2) C1-4 alkyl, (3) C2-4 alkenyl, (4) C2-4 alkynyl, (5) C1-4 alkyl substituted with -OR^{21a}, (6) C1-4 alkyl substituted with -NR^{22a}R^{23a} or

(7)
$$(R^{24a})_{pa}$$
, or

R^{4a} and R^{5a} are taken together with the nitrogen to which they are attached to form a 3-15 membered mono-, bi- or tri-cyclic heteroring, wherein the heteroring represents at least one nitrogen and it may be substituted with C1-4 alkyl substituted with OR^{25a},

 R^{21a} , R^{22a} , R^{23a} and R^{25a} are each independently, (1) hydrogen, (2) C1-4 alkyl, (3) C2-6 acyl, or (4) trihaloacetyl,

E^a is (1) a bond, (2) C1-6 alkylene, (3) C2-6 alkenylene, or (4) C2-6 alkynylene, wherein E^a may be substituted with 1-3 of (1) C1-4alkyl, or (2) C1-4 alkyl substituted with -OR^{26a},

R^{26a} is (1) hydrogen, (2) C1-4 alkyl, (3) C2-6 acyl, or (4) trihaloacetyl, Cyc2^a is (1) C3-15 carboring, or (2) 3-15 membered heteroring having 1-4 of nitrogen, 1-2 of oxygen and/or 1-2 of sulfur,

 R^{24a} is (1) C1-4 alkyl, (2) halogen, (3) cyano, (4) trihalomethyl, (5) $-OR^{27a}$, (6) $-SR^{28a}$, (7) $-NR^{29a}R^{30a}$, (8) nitro, (9) $-COOR^{31a}$, (10) $-CONR^{32a}R^{33a}$, (11) $-NR^{34a}COR^{35a}$, (12) $-SO_2NR^{36a}R^{37a}$, (13) $-NR^{38a}SO_2R^{39a}$, (14) $-S(O)R^{40a}$, or (15) $-SO_2R^{41a}$,

 R^{27a} , R^{28a} , R^{29a} , R^{30a} , R^{31a} , R^{32a} , R^{33a} , R^{34a} , R^{35a} , R^{36a} , R^{37a} , R^{38a} , R^{39a} , R^{40a} and R^{41a} are each independently (1) hydrogen, or (2) C1-4 alkyl,

ia is 0 or an integer of 1 to 5, ma is 0 or an integer of 1 to 4, and na is 0 or an integer of 1 to 4, pa is 0 or an integer of 1 to 5, and wherein when ia is 2 or more, R^{1a}'s are the same or different, when ma is 2 or more, R^{2a}'s are the same or different, when na is 2 or more, R^{3a}'s are the same or different, and when pa is 2 or more, they are the same or different, or a prodrug thereof or a salt thereof.

5. The remedy and/or the preventive according to claim 1, wherein the EDG-2 antagonist is a compound of formula (II)

wherein R^{1b} is C1-20 alkyl optionally having substituent(s), aryl, heteroring, alkyloxy, aryloxy, alkylthio, arylthio, or halogen,

R^{2b} is alkyl optionally having substituent(s), aryl, heteroring, alkyloxy, aryloxy or halogen,

R^{3b} is hydrogen, lower alkyl or halogenated alkyl,

R^{4b} is a group selected from (a) phenyl, aryl or heteroring optionally having substituent(s), (b) substituted or unsubstituted alkyl, and (c) substituted or unsubstituted alkenyl, and

X^b is oxygen or sulfur, and

wherein R^{3b} and R^{4b} may be taken together with the carbon to which they are attached to form a 5-10 membered ring, and

when R^{3b} is hydrogen, R^{4b} is not methyl, or a salt thereof.

6. The remedy and/or the preventive according to claim 1, wherein the EDG-2 antagonist is a compound of formula (III)

$$R^{c}-G^{c}\xrightarrow{T^{c}}J^{c}\xrightarrow{K^{c}-B^{c}}$$

$$Q^{c}\xrightarrow{D^{c}}$$

$$L^{c}\xrightarrow{L^{c}}M^{c}-Z^{c}$$

$$(III)$$

wherein R^c is optionally substituted aliphatic hydrocarbon or a ring group optionally having substituent(s),

G^c is a bond or a spacer having a main chain of 1 to 8 atoms,

T^c is -CH₂- or a spacer having a main chain of 1 atom having a hydrogen bond-accepting group optionally having substituent(s),

J^c is nitrogen or carbon,

B^c is optionally substituted aliphatic hydrocarbon or a ring group optionally having substituent(s),

 K^c is (1) a bond or (2) a spacer having a main chain of 1 to 8 atoms which may form a ring together with the substituent of the ring group represented by R^c , ring D^c or the substituent of the ring D^c ,

 Q^c is (1) a bond or (2) a spacer having a main chain of 1 to 8 atoms which may form a ring together with the ring group represented by R^c , a substituent of the ring group represented by R^c , or K^c ,

ring D^c is a ring optionally having more substituent(s), L^c is a bond or a spacer having a main chain of 1 to 3 atoms, ring E^c is, a ring group optionally having substituent(s), M^c is a bond or a spacer having a main chain of 1 to 8 atoms, Z^c is an acidic group, and t is 0 or 1, or a salt thereof.

- 7. A method for the treatment and/or prevention of a chronic disease characterized by administering to a mammal an effective amount of an EDG-2 antagonist.
- 8. Use of an EDG-2 antagonist for the manufacture of a remedy and/or preventive of a chronic disease.
- 9. A remedy and/or preventive, comprising an EDG-2 antagonist in combination with one or more selected from LPA receptor antagonist, anti-androgenergic agent, α1 receptor blocker or 5α-reductase inhibitor.